Docket No.: K21364USWO (C038435/0184371)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :	)	
Werner BONRATH *et al.*	)	Examiner: Kellette Gale
Serial No.: 10/524,762	)	Art Unit: 1621
Filed: February 15, 2005	)	
For: **ETHYNYLATION PROCESS**	)	

DECLARATION OF DR. WERNER BONRATH UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Werner Bonrath, a citizen and resident of Germany, hereby declare as follows:

1. I studied chemistry at the Universities of Bonn and Münster, Germany from 1979 to 1985.

2. I received a doctorate in Chemistry in 1988 from the Max Planck Institute of Carbon Research, Mülheim an der Ruhr, Germany.

3. In 1988-1989, I was a post-doctoral fellow at the University of Innsbruck, Austria.

4. Since 1989, I have been employed at DSM Nutritional Products, B.V. (previously Roche Vitamins Ltd. and F. Hoffmann-La Roche Ltd.), Basel, Switzerland as a chemist in the research and development department for vitamins and fine chemicals.

5. I am one of the inventors of the invention described and claimed in the captioned application directed to an ETHYNYLATION PROCESS.

6. The present application discloses and claims a process for the manufacture of an acetylenically unsaturated alcohol. The reaction proceeds by reacting a carbonyl compound with acetylene in the presence of ammonia and an alkali metal hydroxide. The carbonyl compound is selected from methyl ethyl ketone, methylglyoxal dimethylacetal, 6-methyl-5-hepten-2-one, 6-methyl-5-octen-2-one, hexahydropseudoionone, 4-(2,6,6-trimethyl-1-cyclohexen-1-yl)-3-buten-2-one, and 6,10,14-trimethyl-2-pentadecanone. The alkali metal hydroxide is used in aqueous solution and the molar ratio of the alkali metal hydroxide to the carbonyl compound is less than 1:200. (Specification, page 1; lines 3-8 and page 2, line 13 page 5, line 2 and claim 1.)

7. I am aware that two Office Actions (Paper Nos. 20060914 and 20070316) have issued with regard to the present application. It is my understanding that in the first Office Action, the Examiner asserted that the claimed process is not patentably distinct from Tedeschi *et al.*, U.S. Patent No. 3,709,946 ("Tedeschi"). (Paper No. 20060914 at 2.) In making this rejection, the Examiner relied on Tedeschi as disclosing "a process for preparing an acetylenic alcohol by reacting a ketone with liquefied

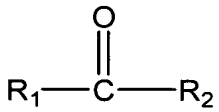
acetylene in the presence of a co-catalyst system comprising liquid ammonia and an alkali metal hydroxide." (Paper No. 20060914 at 2.) The Examiner acknowledged, however, that Tedeschi differs from the claimed invention in that it does not specifically disclose the seven carbonyl compounds recited in, *e.g.*, claim 1. Rather, the Examiner asserted that Tedeschi discloses "that any ketone may be used...." (*Id.* at 3.) In addition, the Examiner acknowledged that, Tedeschi differs from the claimed invention in that Tedeschi discloses "process conditions such as temperature, pressure and concentration [that] may not exactly fall within the claimed ranges." (*Id.*) The Examiner also acknowledged that "Tedeschi does not disclose a continuous process" as claimed. (*Id.*) I also understand that the Examiner concluded that "since Tedeschi et al [discloses] that any ketone can be used in his process of preparing an acetylenic alcohol; it would be obvious ... to prepare such an alcohol using any ketone and expect to arrive at the desired acetylenic alcohol." (*Id.*)

8. It is further my understanding that in the final Office Action the Examiner maintained the rejection over Tedeschi. (Paper No 20070316 at 3.) The Examiner noted that the applicant "claims that the molar ratio of acetone:alkali metal hydroxide[1] [disclosed in Tedeschi] is much more than that claimed by applicant and that applicant claims 'less than 1:200, but wherein the description in Tedeschi et al only goes as low as 1:11.9 which is still greater than that which is claimed." (*Id.*)

[1] The Examiner has apparently reversed the components of the ratio. The correct ratio is a molar ratio of alkali metal hydroxide to carbonyl compound.

9. In view of the foregoing, it is my understanding that the Examiner requires a showing of "unexpected results." (*Id.*) "Tedeschi et al is preparing the same class of compounds as the applicant has claimed; therefore it is not considered to be patentably distinct without a showing of unexpected results." (*Id.*)

10. I am familiar with the Tedeschi document cited by the Examiner. Tedeschi discloses "a process for making acetylenic alcohols which does not require the use of an added solvent medium." (Col. 1, lines 63-65.) Tedeschi discloses that the process "involv[es] the reaction of acetylene with a ketone in the presence of a co-catalyst system." (Col. 1, lines 24-26.) Tedeschi further discloses that "any ketone may be reacted with the liquefied acetylene ... [and that] the preferred ketones have the general formula



wherein R_1 and R_2 may be the same or different radicals selected from the group consisting of hydrogen, alkyl groups containing 1-20 carbon atoms, ... cycloalkyl, and aryl." (Col. 2, lines 19-34.) Tedeschi also discloses that the co-catalyst system is "an alkali metal hydroxide and liquid ammonia." (Col. 1, lines 71-72.) Tedeschi discloses that the "alkali metal hydroxide is used in catalytic quantities, i.e., less than equimolar quantities with respect to the ketone, preferably at most about .5 mole per mole of ketone but at least .001 mole per mole of ketone." (Col. 2, lines 60-64.)

11. To demonstrate that the claimed process is not obvious over Tedeschi, five comparative ethynylation reactions using different carbonyl compounds, described herein, were performed under my supervision and direction. These experiments demonstrate that the claimed process using molar ratios of the alkali metal hydroxide to the carbonyl compound of less than 1:200 produced less than 50% of an unwanted diol by-product compared to processes using molar ratios greater than 1:200, which would not have been expected or predicted by one of ordinary skill in this art at the time the application was filed.

12. The five ethynylation reactions were carried out as follows: potassium hydroxide ("KOH") in a 45% (wt./vol.) aqueous solution and the starting carbonyl ("SC") (reactions shown in Table 1) at the molar ratios shown in Table 2 ("KOH:SC") were introduced into a reaction vessel (a 2 liter autoclave). For each carbonyl compound, three ethynylation reactions were carried out. One reaction wherein the molar ratio of the alkali metal hydroxide to carbonyl compound was within the scope disclosed by Tedeschi and two reactions wherein the molar ratio of the alkali metal hydroxide to carbonyl compound within the scope recited, *e.g.*, claim 1 of the present invention.

13. For each ethynylation reaction, the atmosphere in the reaction vessel was rendered inert by evacuating the air from it and flushing with nitrogen. 369 grams ammonia were then introduced into the reaction vessel. Acetylene was then added to provide a fixed total pressure at 30°C, as shown in Table 2, corresponding to about 21% (wt./wt.) for each reaction. The duration of the reaction was either 1 or 2 hours (Table 2) and the temperature was maintained at 30°C throughout each reaction.

14. At the end of the reaction, the ammonia was evaporated off. The residue in the reaction vessel was acidified with 8% sulphuric acid and washed with water at 60°C while maintaining the pH at 7. The percent conversion of the starting carbonyl into the acetylenically unsaturated alcohol product was determined by gas chromatography. The percentage yield of the product and the percentage yield of the unwanted diol by-product were then determined based on the percent conversion of the product (Table 2).

15. The 5 ethynylation reactions run were:

Reaction	Reaction
1	6-methyl-5-hepten-2-one (MH) to dehydrolinalool (DLL)
2	hexahydropseudoionone (HPI) to 3,7,11-trimethyl-1-dodecyn-3-ol (TMDO)
3	6,10,14-trimethyl-2-pentadecanone (TMPO) to dehydroisophytol (DIP)
4	methyl ethyl ketone (MEK) to 2-ethyl-3-butyn-2-ol (EBO)
5	6-methyl-5-octen-2-one (MOO) to ethyl dehydrolinalool (EDLL)

Table 1. The 5 ethynylation reactions tested.

16. The reaction conditions and results are shown in Table 2:

Reaction	KOH:SC	Duration (h)	Pressure (bar)	Conversion to Product (%)	Product Yield (%)	By-Product Yield (%)	Decrease in By-product Yield (%)
1	1:31	1	16.1	98.0	91.9	3.6	–
	1:250	1	16.1	95.9	92.9	1.4	61
	1:250	2	16.1	97.5	94.3	1.5	58
2	1:27	1	16.3	97.9	94.1	2.5	–
	1:250	1	16.3	96.0	93.7	0.6	76
	1:250	2	16.3	96.9	94.2	0.6	76
3	1:24.5	1	16.8	97.7	94.7	2.0	–
	1:250	1	16.8	95.7	93.3	0.6	70
	1:250	2	16.8	97.2	94.6	0.6	70
4	1:90	1	16.0	99.7	97.6	1.6	–
	1:360	1	16.0	97.1	96.3	0.4	75
5	1:46	1	16.1	97.9	94.4	1.9	–
	1:250	1	16.1	96.5	93.9	0.8	57
	1:250	2	16.1	97.7	95.0	0.9	52

Table 2. Reaction conditions and results (KOH:SC is the ratio of potassium hydroxide to starting carbonyl).

17. As shown in Table 2, at a molar ratio of potassium hydroxide ("KOH") to starting carbonyl ("SC") greater than that claimed in the instant application and within the scope of the ratios disclosed in Tedeschi, the yield of the unwanted diol by-product is from 1.6 % to 3.6%. On the other hand, in the reactions of the invention, the yield of the unwanted diol by-product is from 0.4 % to 1.5%. Thus, the yield of unwanted diol by-product is between 52% and 76% less using the claimed reaction conditions, particularly the molar ratio of the alkali metal hydroxide to the carbonyl compound, as compared to reactions in which the reaction conditions, particularly the molar ratio, is within the scope contemplated by Tedeschi.

18. Based on my knowledge and experience, and in view of the results presented herein, it is my opinion that one of skill in the art at the time the present

invention was made and who was familiar with Tedeschi could not have predicted that the process of the present invention would produce the significantly smaller unwanted diol by-product yields as compared with processes using molar ratios of potassium hydroxide to starting carboxyl compound greater than 1:200, such as the processes of Tedeschi. To further purify the product of the Tedeschi process would require additional time, reagents, and expense. Accordingly, in my opinion, the presently claimed process is surprisingly and unexpectedly superior to processes of the type disclosed in Tedeschi.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: October 1, 2007

Dr. Werner Bonrath